

Claims

*Sch. P.D.*  
1. A combination comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-pyrimidin-2-one or a pharmaceutically acceptable derivative thereof and a second therapeutic agent, bis(pivaloyloxymethyl)(9-[(R)-2-(phosphonomethoxy)ethyl]adenine or a pharmaceutically acceptable derivative thereof wherein (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-pyrimidin-2-one and the second therapeutic agent are present in the range 40:1 to 1:1 by weight.

10 2. A combination according to claim 1 wherein the ratio is in the range 25:1 to 15:1 by weight of active ingredients.

15 3. A combination according to any one of claims 1 to 3 for use in medicine.

20 4. A pharmaceutical formulation comprising a combination according to any one of claims 1 to 3 in association with one or more pharmaceutically acceptable carriers therefor.

25 5. A pharmaceutical formulation for use in the treatment of HBV comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-pyrimidin-2-one or a pharmaceutically acceptable derivative thereof and a second therapeutic agent selected from (9-[(R)-2-(phosphonomethoxy)ethyl]adenine or a pharmaceutically acceptable derivative thereof, and bis(pivaloyloxymethyl)(9-[(R)-2-(phosphonomethoxy)ethyl]adenine or a pharmaceutically acceptable derivative thereof wherein (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-pyrimidin-2-one and the second therapeutic agent are present in the range 40:1 to 1:1 by weight.

30 6. A formulation according to claims 4 or 5 in unit dosage form.

7. A formulation according to any one of claims 4 to 6 suitable for oral administration.

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8. A formulation according to any one of claims 5 to 7 comprising between 25 to 150 mg of lamivudine and 5 to 60 mg adefovir dipivoxil.

9. A formulation according to claim 8 comprising 100 mg of lamivudine and 10 mg adefovir dipivoxil.

10. A method for the treatment of a mammal, including a human, with an HBV infection comprising administration of a therapeutically effective amount of a combination comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-pyrimidin-2-one or a pharmaceutically acceptable derivative thereof and a second therapeutic agent selected from (9-[(R)-2-(phosphonomethoxy)ethyl]adenine or a pharmaceutically acceptable derivative thereof, and bis(pivaloyloxymethyl)(9-[(R)-2-(phosphonomethoxy)ethyl]adenine or a pharmaceutically acceptable derivative thereof.

11. A method as claimed in claim 10 wherein the combination is as claimed in any of claims 1 to 3.

12. A method according to claim 10 or claim 11 wherein the combination is administered simultaneously.

13. A method according to claim 10 or claim 11 wherein the combination is administered sequentially.

25 14. A method according to claim 10 or claim 11 wherein the combination is administered as a single combined formulation.

15. A method as claimed in any one of claims 10 to 14 for the treatment of an HBV infection resistant to nucleoside and/or non-nucleoside inhibitors of the replication of the hepatitis B virus

30 35 16. Use of (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-pyrimidin-2-one in the manufacture of a medicament for administration either simultaneously or sequentially with bis(pivaloyloxymethyl)(9-[2-(phosphonomethoxy)ethyl]adenine, for the treatment of an HBV infection.

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17. Use of bis(pivaloyloxymethyl)(9-[2-(phosphonomethoxy)ethyl]adenine in the manufacture of a medicament for administration either simultaneously or sequentially with (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one for the treatment of an HBV infection.

18. Use of a combination comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-pyrimidin-2-one or a pharmaceutically acceptable derivative thereof and a second therapeutic agent bis(pivaloyloxymethyl)(9-[(R)-2-(phosphonomethoxy)ethyl]adenine or a pharmaceutically acceptable derivative thereof for the treatment of an HBV infection.

19. Use of a combination as claimed in any one of claims 1 to 3 for the treatment of an HBV infection.

20. Use of a combination comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-pyrimidin-2-one or a pharmaceutically acceptable derivative thereof and a second therapeutic agent selected from either (9-[(R)-2-(phosphonomethoxy)ethyl]adenine or a pharmaceutically acceptable derivative thereof, or bis(pivaloyloxymethyl)(9-[(R)-2-(phosphonomethoxy)ethyl]adenine or a pharmaceutically acceptable derivative thereof wherein (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-pyrimidin-2-one and the second therapeutic agent are present in the range 40:1 to 1:1 by weight, for the treatment of an HBV infection resistant to nucleoside and/or nonnucleoside inhibitor.

21. Use of a combination as claimed in any one of claims 1 to 3 for the treatment of an HBV infection resistant to nucleoside and/or nonnucleoside inhibitor of the replication of the hepatitis B virus.

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22. A patient pack comprising of at least one active ingredient selected from (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-pyrimidin-2-one, and bis(pivaloyloxymethyl)(9-[2-(phosphonomethoxy)ethyl]adenine and an information insert containing directions on the use of both active ingredients together in combination.